

## Sporadic viral myositis in two adults

C. David Naylor, MD, DPhil, FRCPC  
Anthony M. Jevnikar, MSc, MD, FRCPC  
Norbert J. Witt, MD, FRCPC

**D**iffuse myalgia is common in the prodromal phase of viral illnesses. However, overt myositis, with weakness and signs of muscle inflammation, rarely accompanies viral infection in adults.<sup>1,2</sup> We report two cases of self-limited myositis in women who presented with contrasting signs and symptoms.

### Case reports

#### Case 1

A 65-year-old woman suffered malaise, nausea, vomiting and watery diarrhea for 3 days. Ten days later she had severe myalgia in the upper trunk and arms and then in the legs. Increasing weakness, difficulty in swallowing and tea-coloured urine were noted over the next 2 days.

The patient's voice was soft, and she could not increase its volume. She had pitting edema of the arms and legs and marked weakness in the hip and shoulder girdles. Her distal muscle strength, sensation and reflexes were normal.

The initial serum creatine kinase level was 73 088 (normally 35 to 230) U/L; the level was still elevated, at 1451 U/L, 3 weeks later. Peritoneal dialysis was briefly required for acute renal failure due to myoglobinuria.

The patient's strength returned slowly over a 4-month period; 7 weeks after the onset of the muscle weakness she was able to do light house-

work, and her serum creatine kinase level was normal.

#### Case 2

A 69-year-old healthy woman suffered a brief bout of rhinitis, sore throat and myalgia 6 weeks before admission. Two weeks later she began to experience lassitude and aching in her proximal muscles after physical activity. Her strength slowly deteriorated until she was unable to walk or comb her hair.

On admission multiple systolic clicks and a midsystolic murmur were detected. There was severe proximal muscle weakness in the patient's arms and legs; her neck muscles were also weak. Pitting edema of the upper arms and thighs was noted.

The serum creatine kinase level was 3832 U/L. Corticosteroid treatment was considered for probable polymyositis but was deferred pending observation for spontaneous resolution of possible viral myositis. By day 15 the creatine kinase level had returned to normal, and it did not change thereafter.

The patient's clinical recovery continued, and full muscle strength was recorded at follow-up 1 and 4 months after discharge. At 14 months she reported that she was feeling well and had suffered no recurrences.

### Diagnostic studies

Serologic testing for various nonbacterial infections was performed in both cases, by means of complement fixation, immunofluorescence or neutralization tests. In case 1 the only evidence of

*From the Department of Medicine, Victoria Hospital and University of Western Ontario, London*

*Reprint requests to: Dr. C. David Naylor, 19 Washington Ave., Toronto, Ont. M5S 1L1*

recent viral infection was an increase in the cytomegalovirus complement fixation titre, from 1:4 to 1:32 over a 3-week period; the tests for adenovirus, influenza A and B viruses, respiratory syncytial virus, herpesvirus, parainfluenza virus types 1 to 3 and coxsackie B viruses yielded negative results. In case 2 the results were positive for respiratory syncytial virus, the complement fixation titres being 1:40 on days 9 and 18, and negative for adenovirus, influenza A and B viruses, and coxsackie B viruses.

Serologic evidence of trichinosis or toxoplasmosis was absent in both cases.

Detailed immunologic screening for evidence of connective tissue diseases yielded negative results. In case 2 the thyroid-stimulating hormone level was elevated, at 13 (normally less than 10) U/L, but her thyroid profile was otherwise normal. The antithyroid antibody titres were increased, which suggested subclinical Hashimoto's thyroiditis.

Electromyograms in both cases showed typical myopathic features in the affected muscles. The results of nerve conduction studies were normal. In case 1 light and electron microscopic examination of a biopsy specimen of the left deltoid muscle, obtained on hospital day 17, revealed many acutely necrotic muscle fibres at various stages of degeneration and scattered infiltration by polymorphonuclear leukocytes and macrophages. The blood vessels were normal. No inclusion bodies or viral particles were seen. The histochemical results were negative.

## Discussion

Neither patient had been exposed to myotoxins, had evidence of connective tissue disease or had a history of muscle dysfunction. Although the serologic studies for viral infection had inconclusive results, the presence of typical prodromal illnesses and the absence of other causes suggested that both cases were related to previous viral infection.

Self-limited viral myositis is more common among children and has been associated with influenza A and B; the symptoms are primarily confined to the calf muscles.<sup>1,2</sup> Among adults Bornholm disease is the best-known clinical example of viral myositis. Accordingly, Hudgson and Walton<sup>3</sup> have stressed that the "cardinal clinical feature of viral myositis is severe muscle pain, particularly in the limb girdles and the paravertebral musculature, with little or no muscle weakness", and recovery within days. Clearly the two patients we have described had a very different clinical syndrome.

A computerized and manual search of the English literature found fewer than 25 similar cases in adults.<sup>4-19</sup> Four features distinguish these sporadic cases from the more usual and benign forms of viral myositis: the muscle weakness is often

marked and tends to spare only the distal muscles; myalgia is present in the prodromal phase, but severe muscle pain is unusual; muscle necrosis is common, as shown by the elevated serum creatine kinase levels, and myoglobinuria can occur; and the condition may progress and resolve slowly, the patient recovering fully in weeks rather than in days.

The cases we have described have shown that the time from the initial symptoms of viral illness to the onset of myositis varies; the literature has shown that the myositis may virtually coincide with the viral infection<sup>4</sup> or develop up to 3 weeks later.<sup>5</sup> Recurrences in one patient were noted, but the reasons were unclear.<sup>6,7</sup> Once symptoms have started, exercise may precipitate rhabdomyolysis,<sup>8,9</sup> and local tissue damage can be intensified by injury to or exercise of specific muscle groups.<sup>10,11</sup>

Previous reports have generally implicated viruses by exclusion and by virtue of a typical prodromal illness. Supportive evidence for a viral illness has been obtained from serologic studies,<sup>4-18</sup> culture of throat swabs<sup>10,12</sup> and culture of stool.<sup>4,7</sup> Only rarely has a virus been isolated from muscle biopsy specimens.<sup>13,14</sup>

Two cases of myositis were reported in association with hepatitis B antigenemia, but the course was more protracted than usual.<sup>20,21</sup> Both patients responded to corticosteroid therapy, although one died soon after of unknown causes. The effect of steroids on other forms of self-limited viral myositis is unknown.

Although the differential diagnosis for this syndrome is long, most disorders can be ruled out by careful history-taking, physical examination and standard laboratory tests. Electromyography findings can confirm myopathy but are nonspecific.<sup>22</sup> Although myonecrosis without an inflammatory-cell infiltrate is often present,<sup>9,10,12,14,17</sup> a typical pathological picture has not been identified, and virus-like particles are unusual.<sup>5</sup>

Chronic polymyositis is the most difficult condition to rule out. Neither muscle biopsy nor electromyography helps. As in case 1 and other reports,<sup>5,13</sup> an inflammatory-cell infiltrate like that in typical polymyositis is occasionally present in self-limited viral myositis. Indeed, these cases could have been diagnosed as "definite" or "probable" polymyositis by the widely accepted criteria of Bohan and associates.<sup>23</sup> Rowland and colleagues<sup>19</sup> have criticized these criteria as being vague and have contended that clinical studies of steroid-responsive polymyositis are "contaminated" by patients with self-limited viral myositis. A recent report on colchicine neuromyopathy also pointed out that patients had been treated unnecessarily with steroids because of the poor criteria for the diagnosis of polymyositis.<sup>24</sup>

For differential diagnostic purposes viral studies may have inconclusive results, as in the two cases we have described, and reports on titres in serum obtained during convalescence to confirm a diagnosis will arrive after the necessary manage-

ment decisions have been made. The specificity of viral markers in diagnosing self-limited myositis is also uncertain in light of the evidence for viral involvement in chronic inflammatory myopathies.<sup>25-30</sup>

We believe that the diagnosis is clinical. No presenting feature is definitive, but the disease should be suspected when a patient presents with weakness of acute or subacute onset, a history of upper respiratory or gastrointestinal tract infection and no other explanation for the inflammatory myopathy. If spontaneous resolution occurs with expectant therapy, the diagnosis of self-limited viral myositis is confirmed, and steroid treatment can be avoided.

As to mechanisms, we speculate that direct viral invasion and disruption of myocytes could account for acute rhabdomyolysis shortly after a prodromal viral illness, whereas a delayed onset of weakness might be due to self-limited autoimmune myositis. Four major pathogenetic possibilities exist for viral involvement in such an autoimmune process: (a) deposition of circulating virus-antibody complexes in muscle, with "innocent bystander" damage; (b) transformation of antigens on muscle membrane by adsorption of viral particles or virus-antibody complexes; (c) virus-induced expression of histocompatibility antigens on the cell surface; and (d) immunologic cross-reactivity as a result of molecular mimicry due to amino acid homology in viral and human muscle proteins.<sup>31</sup>

Continuing advances in molecular biology should help to delineate the pathogenesis of sporadic self-limited myositis and its relation to the chronic inflammatory myopathies.

We thank Professor Joseph J. Gilbert, a neuropathologist at Victoria Hospital, London, Ont., for his expert advice.

## References

1. Mastaglia FL, Ojeda VJ: Inflammatory myopathies [first of two parts]. *Ann Neurol* 1985; 17: 215-227
2. Idem: Inflammatory myopathies [second of two parts]. *Ibid*: 317-323
3. Hudgson P, Walton JN: Polymyositis and other inflammatory myopathies. In Vinken PJ, Bruyn GW (eds): *Diseases of Muscle: Part II* (Handbook of Clinical Neurology, vol 41), North Holland, Amsterdam, 1979: 53-54
4. Wright J, Couchonnai G, Hodges GR: Adenovirus type 21 infection: occurrence with pneumonia, rhabdomyolysis, and myoglobinuria in an adult. *JAMA* 1979; 241: 2420-2421
5. Greco TP, Askenase PW, Kashgarian M: Postviral myositis: myxovirus-like structures in affected muscle. *Ann Intern Med* 1977; 86: 193-194
6. Simon NM, Rovner RN, Berlin BS: Acute myoglobinuria associated with type A2 (Hong Kong) influenza. *JAMA* 1970; 212: 1704-1705
7. Berlin BS, Simon NM, Bovner RN: Myoglobinuria precipitated by viral infection. *JAMA* 1974; 227: 1414-1415
8. Zappacosta AR: Myoglobinuria associated with mononucleosis. *J Am Med Wom Assoc* 1977; 32: 428-430
9. Josselson J, Pula T, Sadler JH: Acute rhabdomyolysis associated with an echovirus 9 infection. *Arch Intern Med* 1980; 140: 1671-1672
10. Schlesinger JJ, Gandara D, Bensch KG: Myoglobinuria associated with herpes-group viral infections. *Arch Intern Med* 1978; 138: 422-424
11. Jehn UW, Fink MK: Myositis, myoglobinemia, and myoglobinuria associated with enterovirus echo 9 infection. *Arch Neurol* 1980; 37: 457-458
12. Zamkoff K, Rosen N: Influenza and myoglobinuria in brothers. *Neurology* 1979; 28: 340-345
13. Gamboa ET, Eastwood AB, Hays AP et al: Isolation of influenza virus from muscle in myoglobinuric polymyositis. *Neurology* 1979; 29: 1323-1325
14. Kessler HA, Trenholme GM, Harris AA et al: Acute myopathy associated with influenza A/Texas/1/77 infection: isolation of virus from a muscle biopsy specimen. *JAMA* 1980; 243: 461-462
15. Morgensen JL: Myoglobinuria and renal failure associated with influenza. *Ann Intern Med* 1974; 80: 362-363
16. Shenouda A, Hatch FE: Influenza A viral infection associated with acute renal failure. *Am J Med* 1976; 61: 697-702
17. Minow RA, Gorbach S, Johnson BL et al: Myoglobinuria associated with influenza A infection. *Ann Intern Med* 1974; 80: 359-361
18. Kantor RJ, Norden CW, Wein TP: Infectious mononucleosis associated with rhabdomyolysis and renal failure. *South Med J* 1978; 71: 346-347
19. Rowland LP, Clark C, Olarte M: Therapy for dermatomyositis and polymyositis. *Adv Neurol* 1977; 17: 65-97
20. Pittsley RA, Shearn MA, Kaufman L: Acute hepatitis B simulating dermatomyositis. *JAMA* 1978; 239: 959
21. Mihas AA, Kirby JD, Kent SP: Hepatitis B antigen and polymyositis. *Ibid*: 221-222
22. Payan J: Electromyography in polymyositis and some related disorders. *Clin Rheum Dis* 1984; 10: 1-79
23. Bohan A, Peter JB, Bowman RL et al: A computer-assisted analysis of 153 patients with polymyositis and dermatomyositis. *Medicine* 1977; 56: 255-286
24. Kuncel RW, Duncan G, Watson D et al: Colchicine myopathy and neuropathy. *N Engl J Med* 1987; 316: 1562-1568
25. Harati Y, Bergman EW, Niakan E: Postviral childhood dermatomyositis in monozygotic twins [abstr]. *Neurology* 1984; 34 (suppl 1): 289
26. Mikol J, Felton-Papaiconomou A, Ferchal F et al: Inclusion-body myositis: clinicopathological studies and isolation of an adenovirus type 2 from muscle biopsy specimen. *Ann Neurol* 1982; 11: 576-581
27. Travers RL, Hughes GRV, Cambridge G et al: Coxsackie B neutralization titres in polymyositis/dermatomyositis [C]. *Lancet* 1977; 1: 1268
28. Christensen ML, Pachman LM, Schneiderman R et al: Prevalence of coxsackie B virus antibodies in patients with juvenile dermatomyositis. *Arthritis Rheum* 1986; 29: 1365-1370
29. Dalakas MC, Pezeshkpour GH, Gravel M et al: Polymyositis associated with AIDS retrovirus. *JAMA* 1986; 256: 2381-2383
30. Chou SM: Inclusion body myositis: A chronic persistent mumps myositis? *Hum Pathol* 1986; 17: 765-777
31. Walker EJ, Jeffrey PD: Polymyositis and molecular mimicry, a mechanism of autoimmunity. *Lancet* 1986; 2: 605-607